# EXHIBIT A

**Expert Report of Steven P. Cohen, M.D.**

MDL No. 2804

Relating to Case Nos. 17-OP-45004 and 18-OP-45090

### D. DURAGESIC, NUCYNTA, AND NUCYNTA ER HAVE FAVORABLE ABUSE PROFILES

In one study that sought to validate a new instrument for opioid abuse potential, the Duragesic reservoir patch had the lowest abuse potential among 14 opioid agonists evaluated (the Matrix patch ranked 11th out of 14, behind Stadol nasal spray (both were behind Suboxone, which is a mixture of buprenorphine and naloxone approved for the treatment of opioid addiction; *Butler et al. Harm Reduct J 2006*). For adverse events, most are comparable to placebo, and because it reaches the bloodstream via transdermal applications, the incidence of gastrointestinal side effects, which are the most common and a principal reason for discontinuation, is less than for medications given orally that transit the gut (*Rausch and Jansen. US Pharm 2012; Boswell et al. J Opioid Manag 2010; Swedish Council on Health Technology Assessment, 2006*). The more recent advent of the matrix patch has improved tolerance of transdermal fentanyl (skin compatibility, comfort, adhesive properties, satisfaction), and possibly reduced abuse potential and risk of accidental overdose (*Freynhagen et al. J Pain Symptom Manage 2005; Margett and Sawyer. Continuing Education in Anaesthesia Critical Care & Pain 2007*).

Compared to other opioids, tolerance develops slower to tapentadol (*Tzschenke et al. Drugs Today 2009; Hartrick and Rozek. CNS Drugs 2011*) and the risk of addiction and diversion have been shown in multiple studies to be significantly lower (*Butler et al. Pain Med 2015; Dart et al. Pain Med 2016; Cepeda et al. J Pain 2013*). Nevertheless, abuse deterrent formulations are available (*Galia et al. J Opioid Manag 2014*).

For the reasons above, I disagree with plaintiffs' expert Dr. Kessler that any of the materials he cites support the conclusion that Janssen misled physicians or others regarding the benefits or risks of Duragesic, Nucynta, or Nucynta ER.

## X. ADDITIONAL STATEMENTS ATTRIBUTED TO JANSSEN BY PLAINTIFFS AND THEIR EXPERTS WERE NOT MISLEADING

In the discussion above, I have indicated my disagreement with several opinions advanced by plaintiffs' experts. I expand on my opinions on related issues here.

### A. EFFECTIVENESS FOR NON-CANCER PAIN

In my opinion the statements that plaintiffs and their experts attribute to Janssen were not deceptive, fraudulent or misleading, and need to be viewed in the context of the extant information and prevailing views in the medical community at the time. As noted above in numerous locations, opioids have been shown to be effective in well-designed placebo-controlled trials for up to 12 weeks for non-cancer pain, and in open-label studies for much longer follow-up periods. Neither non-opioid analgesics for non-cancer pain, nor opioid or non-opioid analgesics for cancer pain, been studied in placebo-controlled trials for more than 12 weeks because of FDA requirements, practical issues (i.e. institutional review board approval) and ethical concerns. In a highly-cited systematic review from 2007, Finnerup et al. found that

contexts (*Pongratz and Spath. MMW Fortschr Med 2001; Worz et al. MMW Fortschr Med 2001*).

**D. DR. THOMAS GILSON**

It is my understanding that Dr. Gilson testified as a representative of Cuyahoga County, during which he stated that the County, in responding to certain defendants' requests, identified certain medical claims involving prescriptions for opioid medications. Two of the criteria used were that the prescriptions were for non-cancer patients and that they were "high dose, that is 120 medical morphine equivalents or higher, which are far more dangerous." I disagree with the description of 120 morphine milligram equivalents (MME) as necessarily "high dose" or "far more dangerous" than other opioid prescriptions. First, the appropriate dose for a patient is highly variable and depends on a number of factors. Second, a 120 MME threshold is arbitrary, especially as to Duragesic. The FDA has approved Duragesic in 25, 50, 75, and 100 mcg/hour doses, yet under the County's criteria all prescriptions for Duragesic except for the 25 mcg/hour patch are "high dose" and "far more dangerous." As made clear by the CMS 2018 MME conversion table and notes (available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Oral-MME-CFs-vFeb-2018.pdf), a 50 mcg/hour patch is 120 MME (50 mcg/hr fentanyl patch X (10 patches/30 days) X 7.2 = 120 MME/day). Third, Dr. Gilson appears to be basing the 120 MME threshold for Duragesic on a conversion table that assumes 100% bioavailability, but this assertion does not account for the well-documented fact that Duragesic is not 100% bioavailable because of various absorption and other issues (*Marguardt et al. Ann Pharmacother 1995; Solassol et al. Oncol Rep 2005*). Fourth, this threshold is also problematic for Nucynta and Nucynta ER, the active ingredient of which is tapentadol. Endnote ix to the 2018 MME conversion table notes, "Tapentadol is a mu receptor agonist and norepinephrine reuptake inhibitor. Oral MMEs are based on degree of mu receptor agonist activity, but it is unknown if this drug is associated with overdose in the same dose-dependent manner as observed with medications that are solely mu receptor agonists."

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Dated: May 10, 2019

Steven P. Cohen, M.D.